

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing

(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION

See paragraph 2 below

International application No.
PCT/EP2004/051693

International filing date (day/month/year)
03.08.2004

Priority date (day/month/year)
06.08.2003

International Patent Classification (IPC) or both national classification and IPC
A61K9/48

Applicant
FONDAZIONE CARLO E DIRCE CALLERIO ONLUS

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/051693

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|------|
| Novelty (N) | Yes: Claims | 1-25 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | 1-25 |
| | No: Claims | |
| Industrial applicability (IA) | Yes: Claims | 1-25 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

Polysaccharide double-layer microcapsules constituted by an outer layer of chitosan and an inner layer of alginate are known in the prior art. However the here claimed microcapsules differ from those in the prior art (see D1) by a significantly lower concentration of chitosan and differentiated concentrations of divalent ions to first harden the alginate droplets (low concentration of 0,5%) and later stabilize the second layer (high concentration of 10-15%). The microcapsules characterized by such process parameters inevitably differ from those of the prior art and are thus novel (Art. 33(2) PCT).

The problem of the invention in view of this closest prior art was to improve the bioadhesion of such microcapsules to the intestinal mucosa and the release of the active agent transported therein. This was obtained by a special combination of concentrations of the constituents in the preparation and shown in comparative examples (see also ex.7).

The prior art is silent on how to improve the bioadhesion or the intestinal release as a function of the preparation of the microcapsules. The found solution was therefore not evident. Subject matter of claims 1-25 thus involve an inventive step (Art. 33(3) PCT).